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Changing the Rules or Changing the Game?

Reflections on the ANPRM and Protection of Human Subjects in Research

Objectives

- The consider the current HHS ANPRM regarding proposed revisions to the Common Rule in light of history and the current environment
- To comment on the merits and challenges of the proposals contained therein
- Suggest some alternatives, where appropriate, that might be worth consideration

Disclosures

- ◉ I am a former government employee
- ◉ I am not an ethicist
- ◉ I have an independent, investigator- initiated research grant from Pfizer, Inc to study the knowledge and preparedness of active clinical investigators
- ◉ I have received an honorarium for giving a lecture to executives at GE Healthcare regarding research risks from the patient's perspective
- ◉ I have no conflicts of interest, financial or otherwise, related to the content of this presentation

It's that time, again...

- 1974 National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research
- 1980 President's Commission for the Study of Ethical Problems in Biomedical and Behavioral Research
- 1994 Advisory Committee on Human Radiation Experiments
- 1995 National Bioethics Advisory Commission

And again...

- 1996 Governmental Accountability Office Report, *Scientific Research: Continued Vigilance Critical to Protecting Human Subjects*
- 1998 Office of the Inspector General Report: *Institutional Review Boards: A Time for Reform*
- 2000 Office of the Inspector General Report, *Protecting Human Research Subjects: Status of Recommendations*
- 2001 Government Accountability Office Report, *Human Subjects Research: HHS Takes Steps to Strengthen Protections, but Concerns Remain*

And again...

- 2002 HHS ANPRM, *Institutional Review Boards: Requiring Sponsors and Investigators to Inform IRBs of Any Prior IRB Reviews*
 - (withdrawn in 2006; “IRB Shopping is not a significant problem”)
- 2007 Office of the Inspector General Report *The Food and Drug Administration’s Oversight of Clinical Trials*
- 2009 Government Accountability Office Report, *Undercover Tests Show the Institutional Review Board System Is Vulnerable to Unethical Manipulation*
- 2009 The Presidential Commission for the Study of Bioethical Issues

Government Accountability?

- “Responsibility for the protection of human subjects in biomedical research exists at three levels:
 - > at the federal level are agencies, such as HHS;
 - > at the institutional level are research institutions, including universities and academic medical centers;
 - > and at the individual investigator level are physicians, scientists, and other professionals.
- Each level plays a role in meeting federal requirements for protecting human research subjects or in ensuring that the requirements are met.”

--GAO Report, 1996

What about Corporate Accountability?

- In a world in which most risky research with human subjects is done by/for corporate entities with a vested financial interest in both the efficiency of the process and the outcome of the studies, what responsibility should those entities bear?
- Can the conflicts of interest inherent in this process be managed effectively?

Mantra or Mandate?

“As our nation invests in science and innovation and pursues advances in biomedical research and health care, it's imperative that we do so in a responsible manner.”

—*President Barack Obama*

The ANPRM: Talking the Talk

- Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators
- “Revisions to the current human subjects regulations are being considered because OSTP and HHS believe these changes would strengthen protections for research subjects.”

The ANPRM: Walking the Walk?

- “Addressing these considerations now is timely and consistent with the President's Executive Order requiring Federal agencies to review existing significant regulations to determine whether they should be modified, streamlined, expanded, or repealed to make the agency's regulatory program more effective or less burdensome in achieving the regulatory objective.”

The Missing OIG Report?

IRBs: A Time for Reform

- Recast federal IRB requirements to grant IRBs greater flexibility and hold them more accountable for results.
- Strengthen continuing protections for human subjects participating in research.
- Enact Federal requirements that help ensure that investigators and IRB members are adequately educated about and sensitized to human-subject protections.

The Missing OIG Report?

IRBs: A Time for Reform

- Help insulate IRBs from conflicts that can compromise their mission in protecting human subjects.
- Recognize the seriousness of the workload pressures that many IRBs face and take actions that aim to moderate them.
- Reengineer the Federal oversight process.

The Current ANPRM: Seven Proposed Changes

- I. Refinement of Risk-Based Protections
- II. Streamlining IRB Review of Multi-Site Studies
- III. Improving Consent Forms/Process
- IV. Strengthening Data Protections to Minimize Information Risks
- V. Improve Data Collection to Enhance System Oversight
- VI. Extension of Scope of the Federal Regulations
- VII. Clarifying and Harmonizing Regulatory Requirements and Agency Guidance

Refinement of Risk-Based Protections



- All steps taken to protect human subjects should be commensurate with the probability and severity of the potential risks associated with the research.
- The major problem is that the available flexibility is not utilized—reactive hyper-protectionism persists!
- There is no “Excuse” for changing the names of the categories— we must use available review and oversight processes more effectively.

Streamlining IRB Review of Multi-Site Studies



- ◉ If there is only going to be one review, it had better be a good one!
- ◉ Accreditation is a potentially valuable tool/solution, but
- ◉ Is it good enough?
- ◉ Will investigators and investigators use it?
- ◉ Can “IRB shopping” be prevented?

Improve Consent Forms/Process



- Duh?! Of course, this is a good idea, but
 - > Can further government interference and regulation fix the problem?
 - > Prescription, proscription and preemption?
 - > What about compliance and oversight?
- The consent form *per se* should be not more than 1-2 pages long and include only essential information—all details should be included in an attached description of the study, risks and potential benefits.

Strengthening Data Protections to Minimize Information Risks



- Perhaps the most innovative and potentially useful/effective proposal of the lot
 - > It could be very helpful if properly executed;
 - > Education and certification will be needed;
 - > Electronic “wizards” might be helpful;
 - > Need for prospective review not eliminated
- Investigators and institutions must be held accountable;
- There must be appropriate oversight and significant penalties for non-compliance
- Registration without prospective review—you don’t wanna go there!

Improve Data Collection to Enhance System Oversight



- This was a good idea when it was proposed a decade ago
 - > It is still a good idea!
 - > Addresses needs on multiple levels
- Real protections could be enhanced by proper data-sharing and monitoring
 - > A question of priorities
 - > Protections for human subjects
 - > Protections for “proprietary information:

Extension of Scope of the Federal Regulations



- ◉ A no brainer!
 - > Will be met with resistance at every turn!
- ◉ Needs to go even further; should include *all* human research regardless of source of funding
 - > Likelihood of adoption strengthened by Guatemalan Incident
 - > Likelihood of adoption weakened by current political climate

Clarify and Harmonize Regulatory Requirements and Agency Guidance



- Unclear and/or conflicting guidance is worse than no guidance at all
- To 'harmonize' is a euphemism for failure to standardize
- The Common Rule was itself an effort to achieve this goal
- Some argue that the Common Rule is now the single greatest impediment to the goal

Clarify and Harmonize Regulatory Requirements and Agency Guidance



- The Common Rule should be scrapped in favor of a single Federal oversight office for all human research.
- The office should be created by executive order and placed within the Office for Science and Technology Policy.
- Its charter must protect it from political and corporate influence with its actions overseen by a standing equivalent of National Bioethics Commission and the Government Accountability Office

Protections for Human Subjects?

- Rules and regulations, in and of themselves, do not, and cannot, protect human subjects from the risks and potential harms of research.
- Neither should rules and regulations deprive individuals and society of the potential benefits of research
- The current compliance-focused approach may be doing more harm than good...

The ANPRM: Too Much or Too Little, Too Late?

- The ANPRM is yet another attempt to tweak a system that is based on flawed assumptions and failed processes
- Radical change, not incremental and marginal change is necessary
- The burdens for preventing harm to research subject should be born by those who do the research—sponsors, institutions and investigators, not IRBs

Is there a way forward?

- ◉ Adopt a new approach based upon professionalism
 - > Being allowed to do research with/on human subjects is a privilege that must be earned through rigorous training and objectively validated, as is currently the case in medicine and psychology
 - > Credentialing and privileges should be risk-based and
 - > All research activities should be subject to oversight and peer-review.

Change the Role of the IRB from Review and Approve to Responsible Oversight

- ◉ All research proposals must address all relevant safety and ethical concerns
- ◉ The investigator should bear primary responsibility for ethical conduct and risk mitigation strategies in his/her research
- ◉ All research should be subject to review by an IRB or its designated agent at any time
- ◉ Investigators who fail to meet their responsibilities lose their privileges
- ◉ Investigators, institutions and sponsors are held accountable for their actions

Doing the right thing... but differently!

- ◎ ***“Integrity is doing the right thing, even if nobody is watching.” --Unknown***
 - Having someone watching sometimes makes it easier to avoid temptation
- ◎ ***“Insanity: doing the same thing over and over again and expecting different results.” --Albert Einstein***
 - Perhaps this is a time to adopt a completely new approach that will foster the behaviors we desire.